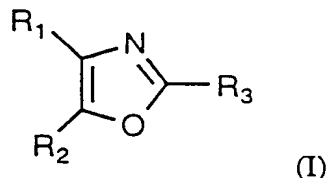


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What is claimed is:

1. A compound of the formula:



wherein:

R₁ and R₂ are independently selected from an optionally substituted aryl or heteroaryl group, provided that at least one of R₁ and R₂ is an optionally substituted heteroaryl, and further provided that both R₁ and R₂ are not the same heteroaryl group;

wherein when one of R₁ and R₂ is an optionally substituted aryl ring, the ring is substituted by one or two substituents, each of which is independently selected, and which, for a 4-phenyl, 4-naphth-1-yl or 5-naphth-2-yl substituent, is halo, cyano, -C(Z)NR₇R₁₇, -C(Z)OR₂₃, -(CR₁₀R₂₀)_m COR₃₆, -SR₅, -SOR₅, -OR₃₆, halo-substituted-C₁₋₄ alkyl, C₁₋₄ alkyl, -ZC(Z)R₃₆, -NR₁₀C(Z)R₂₃, or -(CR₁₀R₂₀)_mNR₁₀R₂₀;

and which, for other positions of substitution, is halo, -(CR₁₀R₂₀)_m-cyano, -C(Z)NR₁₆R₂₆, -C(Z)OR₈, -(CR₁₀R₂₀)_m COR₈, -(CR₁₀R₂₀)_mS(O)_mR₈, -(CR₁₀R₂₀)_mOR₈, halo-substituted-C₁₋₄ alkyl, -C₁₋₄ alkyl, -(CR₁₀R₂₀)_mNR₁₀C(Z)R₈, -(CR₁₀R₂₀)_mNR₁₀S(O)_mR₁₁, -(CR₁₀R₂₀)_mNR₁₀S(O)_mNR₇R₁₇, -(CR₁₀R₂₀)_mZC(Z)R₈ or -(CR₁₀R₂₀)_mNR₁₆R₂₆;

and when one of R₁ and R₂ is an optionally substituted heteroaryl group, the substituent groups include one or two substituents each of which is independently selected from C₁₋₄ alkyl, halo, C₁₋₄ alkoxy, C₁₋₄ alkylthio, NR₁₀R₂₀, or an N-heterocyclyl ring which ring has from 5 to 7 members and optionally contains an additional heteroatom selected from oxygen, sulfur or NR₂₂;

R₃ is -X_aP(Z)(X_bR₁₃)₂, X_c or -(CR₁₀R₂₀)_n R₄;

R₄ is Q-(Y₁)_t;

Q is an aryl or heteroaryl group;

X_c is hydrogen, -(CR₁₀R₂₀)_n (Y₂)_p, -(CR₁₀R₂₀)_n -C=C- (CR₁₀R₂₀)_n (Y₂)_p, -(CR₁₀R₂₀)_n -C≡C- (CR₁₀R₂₀)_n (Y₂)_p, or halosubstituted C₁₋₁₀ alkyl;

t is an integer having a value of 1 to 3;

p is 0 or an integer having a value of 1, provided that when p is 0 then Y₂ is hydrogen;

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- X_a is $-NR_8-$, $-O-$, $-S-$ or a C_{1-10} alkylene chain optionally substituted by C_{1-4} alkyl and optionally interrupted by $-NR_8-$, $-O-$ or $-S-$;
- X_b is independently selected from $-(CR_{10}R_{20})_n$, $-NR_8-$, $-O-$ or $-S-$;
- Z is oxygen or sulfur;
- 5 n is 0 or an integer having a value of 1 to 10;
- n' is an integer having a value of 1 to 10;
- m is 0, or the integer 1 or 2;
- m' is 1 or 2;
- m'' is 0 or an integer having a value of 1 to 5;
- 10 Y_1 is independently selected from hydrogen, C_{1-5} alkyl, halo-substituted C_{1-5} alkyl, halogen, $-X_a-P(Z)-(X_bR_{13})_2$ or $-(CR_{10}R_{20})_nY_2$;
- Y_2 is halogen, $-OR_8$, $-NO_2$, $-S(O)_{m'}R_{11}$, $-SR_8$, $-S(O)_{m'}NR_8R_9$, $-NR_8R_9$, $-O(CR_{10}R_{20})_{n'}NR_8R_9$, $-C(O)R_8$, $-CO_2R_8$, $-CO_2(CR_{10}R_{20})_{n'}CONR_8R_9$, $-ZC(O)R_8$, $-CN$, $-C(Z)NR_8R_9$, $-NR_{10}C(Z)R_8$, $-C(Z)NR_8OR_9$, $-NR_{10}C(Z)NR_8R_9$,
- 15 $-NR_{10}S(O)_{m'}R_{11}$, $-N(OR_{21})C(Z)NR_8R_9$, $-N(OR_{21})C(Z)R_8$, $-C(=NOR_{21})R_8$, $-NR_{10}C(=NR_{15})SR_{11}$, $-NR_{10}C(=NR_{15})NR_8R_9$, $-NR_{10}C(=CR_{14}R_{24})SR_{11}$, $-NR_{10}C(=CR_{14}R_{24})NR_8R_9$, $-NR_{10}C(O)C(O)NR_8R_9$, $-NR_{10}C(O)C(O)OR_{10}$, $-C(=NR_{13})NR_8R_9$, $-C(=NOR_{13})NR_8R_9$, $-C(=NR_{13})ZR_{11}$, $-OC(Z)NR_8R_9$, $-NR_{10}S(O)_2CF_3$, $-NR_{10}C(Z)OR_{10}$, 5-(R_{18})-1,2,4-oxadiazol-3-yl or 4-(R_{12})-5-($R_{18}R_{19}$)-4,5-dihydro-1,2,4-oxadiazol-3-yl;
- 20 R_5 is hydrogen, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl or NR_7R_{17} , excluding the moieties $-SR_5$ being $-SNR_7R_{17}$ and $-SOR_5$ being $-SOH$;
- R_6 is C_{1-4} alkyl, halo-substituted- C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl or C_{3-5} cycloalkyl;
- 25 R_7 and R_{17} is each independently selected from hydrogen or C_{1-4} alkyl or R_7 and R_{17} together with the nitrogen to which they are attached form a heterocyclic ring of 5 to 7 members which ring optionally contains an additional heteroatom selected from oxygen, sulfur or NR_{22} ;
- R_8 is hydrogen, heterocyclyl, heterocyclylalkyl or R_{11} ;
- 30 R_9 is hydrogen, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-7} cycloalkyl, C_{5-7} cycloalkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl or R_8 and R_9 may together with the nitrogen to which they are attached form a heterocyclic ring of 5 to 7 members which ring optionally contains an additional heteroatom selected from oxygen, sulfur or NR_{12} ;
- 35 R_{10} and R_{20} is each independently selected from hydrogen or C_{1-4} alkyl;
- R_{11} is C_{1-10} alkyl, halo-substituted C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-7} cycloalkyl, C_{5-7} cycloalkenyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;

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- R₁₂ is hydrogen, -C(Z)R₁₃ or optionally substituted C₁₋₄ alkyl, optionally substituted aryl or optionally substituted aryl-C₁₋₄ alkyl;
R₁₃ is hydrogen, C₁₋₁₀ alkyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;
- 5 R₁₄ and R₂₄ is each independently selected from hydrogen, alkyl, nitro or cyano;
R₁₅ is hydrogen, cyano, C₁₋₄ alkyl, C₃₋₇ cycloalkyl or aryl;
R₁₆ and R₂₆ is each independently selected from hydrogen or optionally substituted C₁₋₄ alkyl, optionally substituted aryl or optionally substituted aryl-C₁₋₄ alkyl, or together with the nitrogen which they are attached form a heterocyclic ring of 5 to 7 members
10 which ring optionally contains an additional heteroatom selected from oxygen, sulfur or NR₁₂ ;
R₁₈ and R₁₉ is each independently selected from hydrogen, C₁₋₄ alkyl, substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl or together R₁₈ and R₁₉ denote a oxygen or sulfur;
- 15 R₂₁ is hydrogen, a pharmaceutically acceptable cation, C₁₋₁₀ alkyl, C₃₋₇ cycloalkyl, aryl, aryl C₁₋₄ alkyl, heteroaryl, heteroarylalkyl, heterocyclyl, aroyl, or C₁₋₁₀ alkanoyl;
R₂₂ is R₁₀ or C(Z)-C₁₋₄ alkyl;
R₂₃ is C₁₋₄ alkyl, halo-substituted-C₁₋₄ alkyl, or C₃₋₅ cycloalkyl;
R₃₆ is hydrogen or R₂₃;
- 20 or a pharmaceutically acceptable salt thereof.
2. The compound according to Claim 1 wherein R₁ or R₂ is an optionally substituted 4-pyridyl or 4-pyrimidinyl.
- 25 3. The compound according to Claim 2 wherein the optional substituent is C₁₋₄ alkyl or NR₁₀R₂₀.
4. The compound according to any of Claims 1 to 3 wherein R₁ or R₂ is an optionally substituted phenyl.
- 30 5. The compound according to Claim 4 wherein the one or more optional substituents are independently selected from halogen or methoxy.
6. The compound according to any of Claims 1 to 5 wherein R₃ is X_C or
35 -(CR₁₀R₂₀)_nR₄.

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7. The compound according to Claim 6 wherein R₃ is hydrogen, -(CR₁₀R₂₀)_n(Y₂)_p, -(CR₁₀R₂₀)_n CH₃; and Y₂ is -NR₈R₉ or -NR₁₀C(Z)R₈; and R₄ is an optionally substituted phenyl.
- 5 8. The compound according to Claim 5 or 6 wherein R₃ is hydrogen, methyl, amino, -NR₁₀C(O)R₈, phenyl, or phenyl substituted by -SR₈ or -S(O)_mR₁₁.
9. The compound according to Claim 1 which is:
5-(3-Methoxyphenyl)-2-methyl-4-(4-pyridyl)oxazole;
10 5-(4-Fluorophenyl)-2-methyl-4-(4-pyridyl)oxazole;
2-Methyl-4-(Phenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-methyl-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-phenyl-5-(4-pyridyl)oxazole;
2-Amino-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole.
15 4-(4-Fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-methylpyrid-4-yl)oxazole;
4-(3,4-Dichlorophenyl)-5-(4-pyridyl)oxazole;
4-(3-Chlorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-(4-methylthiophenyl)-5-(4-pyridyl)oxazole;
20 4-(4-Fluorophenyl)-2-[4-(methylsulfinyl)phenyl]-5-(4-pyridyl)oxazole;
2-Acetamido-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-amino-pyrimidin-4-yl)oxazole; or pharmaceutically acceptable salts thereof.
- 25 10. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent and a compound according to any of Claims 1 to 9.
11. A method of treating a cytokine mediated disease in an animal in need thereof which method comprises administering to said animal an effective cytokine mediating
30 amount of a compound according to any of Claims 1 to 9.
12. The method according to Claim 11 wherein the cytokine mediated disease is asthma, adult respiratory distress syndrome, stroke, bone reabsorption diseases, arthritic joint conditions, and other inflammatory diseases.
- 35 13. The method according to Claim 11 or 12 wherein the compound is 5-(3-Methoxyphenyl)-2-methyl-4-(4-pyridyl)oxazole;

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- 5-(4-Fluorophenyl)-2-methyl-4-(4-pyridyl)oxazole;
2-Methyl-4-(Phenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-methyl-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-phenyl-5-(4-pyridyl)oxazole;
5 2-Amino-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-methylpyrid-4-yl)oxazole;
4-(3,4-Dichlorophenyl)-5-(4-pyridyl)oxazole;
4-(3-Chlorophenyl)-5-(4-pyridyl)oxazole;
10 4-(4-Fluorophenyl)-2-(4-methylthiophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-2-[4-(methylsulfinyl)phenyl]-5-(4-pyridyl)oxazole;
2-Acetamido-4-(4-fluorophenyl)-5-(4-pyridyl)oxazole;
4-(4-Fluorophenyl)-5-(2-amino-pyrimidin-4-yl)oxazole; or pharmaceutically acceptable
salts thereof.
- 15
14. The method according to any of Claims 11 to 13 wherein the mediation of the
disease state is by Interleukin-1 (IL-1).
15. The method according to any of Claims 11 to 13 wherein the mediation of the
20 disease state is by Tumor Necrosis Factor (TNF).
16. A method of treating inflammation in a mammal in need thereof which comprises
administering to said mammal an effective amount of a compound according to any of
Claims 1 to 9.